Previously considered to have an irreparable condition, 42% of patients had improvement in their vision, with 19% returning to near-normal visual function. Continuing refinements in surgical techniques suggest that substantially better success rates may be expected. Surgical prophylaxis for impending macular holes, when visual symptoms and clinical signs may be subtle yet reversible, is the subject of an ongoing multicenter, prospective clinical trial.

Successful macular hole operations have cast doubt on previous concepts of vitreomacular pathophysiology based on clinical evaluation. Detachment of the vitreous from the surface of the macula is a common and typically benign age-related event. It is now recognized, however, that the exact relationship of the posterior vitreous to the macula can often be determined only at the time of surgical intervention. The most careful preoperative evaluation has frequently been found at the time of a macular operation to be misleading and unreliable, either not recognizing or underestimating the role of the vitreous in the pathologic process. Other disorders, such as loss of vision due to anteroposterior vitreomacular traction caused by incomplete vitreous detachment from the macula, have been recognized and shown to be responsive to surgical intervention. Indeed, it is increasingly appreciated that macular pucker, as well as tangential and anteroposterior vitreomacular traction, may occur alone or in concert, even superimposed on other macular disease, causing or contributing to loss of central vision that may be amenable to surgical intervention.

The development of neovascular membranes beneath the macula is an important cause of central vision loss in a multitude of disorders, particularly the presumed ocular histoplasmosis syndrome and, more commonly, age-related macular degeneration. Recently the surgical removal of submacular neovascular membranes complicating presumed ocular histoplasmosis syndrome and age-related macular degeneration has been reported with encouraging, occasionally remarkable, results. Such developments have ushered in a new era in vitreoretinal surgical treatment by revolutionizing our understanding of clinical vitreomacular pathophysiology and expanding the application of current microsurgical techniques to macular diseases until only recently unrecognized, misunderstood, or considered irreparable.

JEFFREY K. LUTTRULL, MD
Ventura, California

REFERENCES

Gass JDM: Idiopathic senile macular hole—Its early stages and pathogenesis. Arch Ophthalmol 1988; 106:629-639

Kelly NE, Wendel RT: Vitreous surgery for idiopathic macular holes. Arch Ophthalmol 1991; 109:654-659

Lambert HM, Capone A, Aaberg TM, Sternberg P, Mandell BA, Lopez PF: Surgical excision of subfoveal neovascular membranes in age-related macular degeneration. Am J Ophthalmol 1992; 113:257-262

Lewis H, Abrams GW, Blumencranz MS, Campo RV: Vitrectomy for diabetic macular traction and edema associated with posterior hyaloidal traction. Ophthalmology 1992; 99:753-759

Thomas MA, Kaplan HJ: Surgical removal of subfoveal neovascularization in the presumed ocular histoplasmosis syndrome. Am J Ophthalmol 1991; 111:1-7

Laser Treatment of Diabetic Retinopathy

DIABETES MELLITUS is the leading cause of blindness in working-age Americans and accounts for 8,000 cases of new blindness each year in the United States. "Diabetes 2000" is an ambitious, long-term education project of the American Academy of Ophthalmology, designed to eliminate preventable blindness from cases of diabetes by the year 2000. Ophthalmologists and primary care physicians must share advances to accomplish this goal.

Two distinct forms of diabetes mellitus are recognized—juvenile onset (type I) and adult onset (type II). Furthermore, two distinct forms of diabetic retinopathy that may cause blindness occur—proliferative diabetic retinopathy and diabetic macular edema. Proliferative diabetic retinopathy consists of neovascular tissue that grows on the surface of the retina and into the vitreous cavity. If untreated, bleeding occurs into the vitreous, which then contracts, sometimes resulting in retinal detachment. Diabetic macular edema is caused by incompetent vessels leaking serum and lipid into a poorly perfused central retina. As retinal thickening occurs, photoreceptor function decreases and central vision is compromised. Juvenile-onset diabetes carries a higher risk of severe proliferative retinopathy, but because there are more cases of adult-onset diabetes, the latter group comprises a significant proportion of patients with blindness. In many instances, blindness from diabetes can be prevented by early detection and prompt photocoagulation treatment.

In 1976 a National Eye Institute (NEI)-funded Diabetic Retinopathy Study showed that panretinal scatter photocoagulation reduced the rate of profound loss of vision from severe proliferative diabetic retinopathy by 50%. Results are lasting: Of high-risk patients who had a favorable response to photocoagulation, 80% maintained 20/40 (reading) vision five years after treatment. The effects of photocoagulation on the management of less severe stages of diabetic retinopathy were not known until recently. A second NEI clinical trial showed that early treatment, when compared with observation only, was associated with a small reduction in the incidence of severe vision loss, but five-year rates of loss of vision were low in both the early treatment and observation groups. Therefore, if careful follow-up can be maintained, scatter photocoagulation is not recommended for eyes with mild or moderate nonproliferative diabetic retinopathy. When retinopathy is more severe, scatter photocoagulation should be considered and should not be delayed if the eye has reached the high-risk proliferative stage.

Diabetic macular edema is a more common cause of severe loss of vision than proliferative diabetic retinopathy. For eyes with macular edema, focal macular photocoagulation is the only effective treatment that reduces the risk of moderate visual loss. Treatment should be considered only for eyes with clinically significant macular edema, such as edema that involves or threatens the center of the macula. Focal treatment stabilizes visual acuity, increases the chance of visual improvement, decreases the rate of subsequent loss of vision by decreasing the frequency of persistent macular edema, and causes only minor visual field loss. Timing is therefore important. Treatment should ideally be applied before serious vision loss occurs.

Photocoagulation has been proved to be cost effective. A computer-simulation model was designed to predict the economic effects of the treatment of diabetic retinopathy in juvenile diabetes. Using treatment recommendations provided by these clinical trials, the model predicted a cost savings of $9,571 per year for each new patient diagnosed and appropriately treated. If all patients with diabetes mellitus received appropriate care, the predicted annual savings would exceed $167 million and 79,236 person-years of sight. Unfortunately, it is estimated that 22% of patients with type I diabetes and 40% of those with type II diabetes are not obtaining

appropriate eye care. It is less expensive to provide preventive care than to support subsequent disability and its associated personal and social suffering.

Using the results of these clinical trials, a treatment plan for diabetic retinopathy has been designed and proved medically and cost effectively. The trials have shown that most patients with diabetes go blind because they are treated too late. They must be evaluated early to reap the benefits of these studies.

PAUL E. TORNAMBE, MD
La Jolla, California

REFERENCES

Early Treatment Diabetic Retinopathy Study Research Group: Early photocoagulation for diabetic retinopathy—ETDRS Report Number 9. Ophthalmology 1991; 98(suppl):766-785

Early Treatment Diabetic Retinopathy Study Research Group: Early treatment diabetic retinopathy study design and baseline patient characteristic—ETDRS Report Number 7. Ophthalmology 1991; 98(suppl):741-753

Javitt JC, Canner JK, Sommer A: Cost effectiveness of current approaches to the control of retinopathy in type I diabetics. Ophthalmology 1989; 96:255-264

Klein R, Klein BE, Moss SE, Davis MD, DeMets DL: The Wisconsin Epidemiologic Study of Diabetic Retinopathy: X. Four-year incidence and progression of diabetic retinopathy when age at diagnosis is 30 years or more. Arch Ophthalmol 1989; 107:244-249

Vander JF, Duker JS, Benson WE, Brown GC, McNamara JA, Rosenstein RB: Long-term stability and visual outcome after favorable initial response of proliferative diabetic retinopathy to panretinal photocoagulation. Ophthalmology 1991; 98:1575-1579

Retinitis Pigmentosa—New Advances in Ophthalmic Genetics

RETINITIS PIGMENTOSA is both clinically and genetically heterogeneous. It comprises a group of X-linked autosomal recessive and autosomal dominant diseases that affect 50,000 to 100,000 people in the United States, with the incidence ranging from 1 in 3,000 to 1 in 7,000. The early symptoms of retinitis pigmentosa include night blindness and a loss of peripheral fields of vision. As the condition progresses, visual acuity and central vision are also affected. Examination of the fundus reveals attenuated retinal vessels, bone-spicule pigment around the periphery of the retina, and occasionally pale optic discs.

Molecular biologic studies have defined the genetic defects for at least some of the persons and families who have autosomal-dominant retinitis pigmentosa. Most of the mutations discovered to date are the result of changes in a single nucleotide in the rhodopsin gene. Different families may carry different mutations, but affected members of the same family carry the same dominantly inherited mutation. These mutations lead to single amino acid changes in the rhodopsin molecule. The first mutation discovered was a C-to-A base change in the 23rd codon of the rhodopsin gene that resulted in a substitution in the 23rd amino acid of histidine for proline. This mutation was denoted as the proline-23-histidine mutation. In a recent report of 161 unrelated patients with autosomal-dominant retinitis pigmentosa who were screened, 26 (24%) were found to carry a point mutation in the rhodopsin gene. This study described 13 different mutations at 12 different amino acid positions. Research is under way to uncover the molecular defects in the rest of these patients by exploring the possibility of defects in other retinal and photoreceptor genes, such as arrestin (also known as S antigen), transducin, peripherin, and others.

Many investigators have attempted to correlate observed genetic heterogeneity with variability in the clinical severity and prognosis of autosomal-dominant retinitis pigmentosa. Initial observations suggested that patients with certain mutations, such as proline-23-histidine, threonine-58-arginine, glycine-182-serine, and threonine-17-methionine, may have better long-term prognoses than others for the retention of good visual acuity and functional peripheral visual fields. In patients with the proline-347-leucine mutation, there is an increased likelihood of more severe functional impairment. The age of onset and severity of the disease, however, may vary substantially among patients with the same mutation.

How can these new discoveries be used to diagnose and treat patients with retinitis pigmentosa? Molecular genetics, in conjunction with a review of family history and careful clinical examination, can in some cases determine whether a person with a family history of autosomal-dominant retinitis pigmentosa is carrying the disease gene while asymptomatic. This information can assist persons in making career and family choices. The application of further clinical and basic research will one day help to decipher the biochemical basis for retinal degeneration in retinitis pigmentosa, which we hope will lead to a rational basis for treating the disorder. Further research is also required to determine the molecular defect in the great majority of persons with dominantly inherited retinitis pigmentosa, as well as in patients with the autosomal recessive and X-linked type. Patients with this disorder optimally should be referred to centers with experience in its diagnosis and treatment and be enrolled in clinical studies.

VINH TAN TRAN, MD, PhD
Los Angeles, California

REFERENCES

Berson EL, Rosner B, Sandberg MA, Dryja TP: Ocular findings in patients with autosomal dominant retinitis pigmentosa and a rhodopsin gene defect (Pro-23-His). Arch Ophthalmol 1991; 109:92-101

Dryja TP, McGee TL, Reichel E, et al: A point mutation of the rhodopsin gene in one form of retinitis pigmentosa. Nature 1990; 343:364-366

Fishman GA, Stone EM, Sheffield VC, Gilbert LD, Kimura AE: Ocular findings associated with rhodopsin gene codon 17 and codon 182 transition mutations in dominant retinitis pigmentosa. Arch Ophthalmol 1992; 110:54-62

Sung CH, Davenport CM, Hennessey JC, et al: Rhodopsin mutations in autosomal dominant retinitis pigmentosa. Proc Natl Acad Sci USA 1991; 88:6481-6485

Current Therapy for Disorders of the Optic Nerve

OPTIC NEURITIS is characterized by subacute unilateral loss of central vision in patients younger than 40 years, associated with pain on eye movement, diminished pupillary response, and optic disc edema in about 40%. It may be associated with systemic disorders such as systemic lupus erythematosus and syphilis and may be mimicked by parasellar tumors. Most cases are idiopathic, in which there may be a strong association with multiple sclerosis. The value of corticosteroid therapy in idiopathic optic neuritis has not been proved. Early reports indicated that treatment reduced pain and increased the speed of visual recovery but did not appreciably affect the final level of visual acuity. Most neuro-ophthalmologists have treated only those patients with severe pain or with a definitive need for the rapid recovery of vision, such as patients with severe loss of vision, or only one functional eye. The recent national multicenter clinical trial of systemic corticosteroid use in optic neuritis (Optic Neuritis Treatment Trial) showed that oral prednisone therapy alone had no beneficial effect and was associated with an increased risk of recurrence; study investigators have therefore recommended against its use. An initial course of intravenous methylprednisolone sodium succinate, however, followed by oral prednisone was beneficial in patients with visual acuity worse